III. REMARKS

A. STATUS OF THE CLAIMS

Claims 1-3 and 5-20 were pending in this application, and all claims have been rejected.

Claims 6, 17, and 20 have been canceled by this amendment.

Claim 4 was previously canceled.

Claims 1-3, 5, 7-16, 18 and 19 are amended herein.

The foregoing claim amendments were made solely in an effort to expedite prosecution and allowance of the present application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Accordingly, upon entry of the present amendment and response, claims 1-3, 5, 7-16, 18 and 19 will be pending.

Applicant acknowledges with appreciation the Examiner's withdrawal of the previous:

- rejection of claim 1 under 35 USC §112, 2nd paragraph, regarding the "two ionic components";
- rejection of claim 5 under 35 USC §112, 2nd paragraph, regarding the two ionic components";
- rejection of claims 10-11 under 35 USC §112, 1st paragraph, for reciting "about",

Applicant believes that *no new matter has been added* to the claims by these amendments.

B. CLAIM OBJECTIONS

Claim 6 has been canceled, rendering the objection of claim 6 moot.

C. 35 U.S.C. §112 SECOND PARAGRAPH REJECTIONS

Claims 1-3 and 5-20 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant respectfully traverses this rejection. Claims 6, 17 and 20 have been canceled, rendering the rejection of these claims moot

a) Applicant amended claims 1, 5, 7, and 8 to clarify inconsistencies pertaining to the language used to claim the "selected ionic protein component".

b) The Office Action alleges that the meaning of the phrase, "in the absence of an added salt that binds the ionic adsorbent", as recited in claims 1, 12, and 15 is unclear.

Without acquiescing to the validity of this rejection, and solely in an effort to expedite prosecution and allowance of the pending claims, Applicant has amended claims 1, 12, and 15 by deleting the phrase "in the absence of an additional salt that binds with the ionic adsorbent".

Applicant submits that claims 1-3 and 5, 7-16, 18, and 19 meet the specific requirements of 35 U.S.C. §112, second paragraph, and respectfully requests reconsideration and withdrawal of this rejection.

D. 35 U.S.C. §112 FIRST PARAGRAPH REJECTIONS

1. Claims 1-3 and 5-20 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

The Office Action asserts that:

> "claims 1-3 and 5-20 contain subject matter which was not described in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Office Action concludes that Applicant's original disclosure has failed to adequately describe what is *meant* by the phrase "*in the absence of an added salt that binds the ionic adsorbent*". The Office Action maintains that: "In its *literal sense* one could only interpret [the phrase] "in the absence of an added salt that binds the ionic adsorbent" to mean that *absolutely no added salt is present in step a)* of claims 1, 12 and 15. However when one reads the disclosure, it is clear that the "sample" is not devoid of "added salt"..."
>
> The Office Action concludes that, "The teachings therein fail to state what the composition or concentration of the buffer might be. Whatever the composition and concentration thereof, there must inherently be some positive ions that would bind to a cation exchange matrix/adsorbent...This is necessarily true for any kind of buffer, other than an acetate buffer." Thus, the Office Action asserts that the, "sample" of Example 1 *must have inherently had Na+ (or K+) ions added thereto*, and these positive ions would certainly have been able to bind to the SP cationic groups of the matrix/adsorbent". The Office Action asserts that "Applicant, however, has not provided the composition or concentration of the buffer; therefore, one has no idea what Applicant might have contemplated as being the permissible range and/or upper limit of concentration for a positive charged ion that can bind to the matrix/adsorbent."
>
> The Office Action continues..."that Applicant has contemplated separation of biomolecules from complex mixtures...It is necessarily true that whole blood, or plasma derived therefrom...would contain positive ions such as Na+ and K+"...
>
> Therefore, the Office Action concludes that "for these samples, there are inherently positive ions would certainly be able to bind to cationic groups of any cation exchanging matrix/adsorbent. In this case, the examiner grants that there is an "*absence of an added salt*"; *however since salt is inherently present*, then one can contemplate that Applicant's invention would also be operative if a man-made "sample" also contains an "added salt" -- e.g. as in the case in which a protein precipitate is redissolved in a buffer, in the case in which a protein has been eluted from a Protein A matrix".

> Finally, the Office Action concludes that, "[S]ince Applicant has *not adequately described* what "*in the absence of an added salt that binds the ionic adsorbent*" means in actual quantitative terms, one of skill cannot envision what kind of "sample" is or is not within the scope of the invention...one cannot possibly determine what applicant has described as being his invention". The Office Action additionally concludes that "[S]ince Applicant has *not adequately described* what "*in the absence of an added salt that binds the ionic adsorbent*" means in actual quantitative terms, one of skill cannot envision what kind of "sample" is or is not within the scope of the invention.

Applicant respectfully traverses this rejection for the reasons set forth *infra*.

Applicant contends that the specification need not describe the claimed invention in *ipsis verbis* to comply with the written description requirement. *Ex parte* Sorenson, 3 USPQ2d 1462, 1463 (Bd. Pat. App. & Inter. 1987). According to the Patent and Trademark Office Board of Patent Appeals and Interferences in *Ex parte Sorenson*, the test for determining whether a claimed invention is adequately described in the specification is whether the originally filed disclosure *reasonably conveys to a person having ordinary skill in the art that the applicant had possession of the subject matter later claimed. Id.* The Board also stated that the inquiry into whether the description requirement is met is a question of fact and must be determined on a case-by-case basis. *Id* Applicant respectfully traverses this rejections for the following reasons.

Applicant respectfully contends that the specification, in this case, teaches the meaning of the phrase "in the absence of an added *(i.e., competing)* salt (i.e., *an added ionic component that competitively*) that binds the ionic adsorbent", and that the specification as originally filed *reasonably conveys to a person having ordinary skill in the art that the applicant had possession of the subject matter later claimed.* Applicant respectfully contends that the Office Action is taking the phrase *"in the absence of an added salt that binds the ionic adsorbent"* out of context as used and explained throughout the specification.

However, without acquiescing to the validity of this rejection and solely in an effort to expedite prosecution and allowance of the pending claims, Applicant has amended claims 1, 12 and 15 by deleting the phrase "in the absence of an added salt that binds the ionic adsorbent", thereby rendering this rejection moot. Accordingly, Applicant respectfully requests reconsideration and withdrawal of this rejection.

2. Claims 1-3 and 5-20 are rejected under 35 U.S.C. 112, first paragraph, because, allegedly, "*the best mode contemplated by the inventor has not been disclosed. Evidence of concealment* of the best mode is based upon the fact that Applicant has not provided the composition or concentration of the buffer used in Example 1; therefore, one has no idea what applicant might have contemplated as being the permissible range and/or upper limit of concentration for a positive charged ion that can bind to the matrix/adsorbent." Applicant respectfully traverses this rejection for the reasons set forth *infra*.

Again it appears that the Office Action is taking an expression (i.e., buffered solution) from the application out of context. Example 1, in the specification, teaches in-part, "Immunoglobulin G and protein A were mixed in the ratio 10:1 (w/w) in a buffered solution, pH

4.0-5.5 and conductivity 2-6 mSi/cm...". Applicant respectfully contends that the Office Action fails to appreciate that one of ordinary skill in the art, supplied with the teaching in Example 1, would readily and easily be able to reproduce a buffered solution having this criteria. As such, it is clear from the legal precedent that, a patent need not teach, or preferably omits, what is well known in the art. *See*, for example, *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); MPEP §2164.01. Accordingly, one of ordinary skill in the art would have readily known how to reproduce a solution of IgG and protein A, mixed in the ratio 10:1 (w/w) in a buffered solution, having a pH 4.0-5.5 and conductivity 2-6 mSi/cm" as taught in Example 1, and accordingly, claims 1-3 and 5-20 are not rejected under 35 U.S.C. 112, first paragraph,.

For example, Applicant notes that it was well known in the art at the time of the invention that when the ratio of the inside diameter to the outside diameter of a spout, for example, is >0.2, a drop would adhere to the outside diameter. This is further evidenced by ..... It was also well known in the art at the time of the invention, that, the radius of a drop remains the same for a given type of fluid when the ratio of the inside diameter to the outside diameter is >0.2.

3. Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as allegedly, "failing to comply with the written description requirement."

The Office Action maintains that:

> "[T]he claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 20 contains new matter. Specifically, claim 20 does not specify whether it is the "protein A" or the "immunoglobulin" biomolecule that is the one which is the "selected ionic biomolecule" of base claim 15. On the other hand, the original specification and original claim 8 only present the embodiment in which protein A is other than the "selected biomolecule". New claim 20 thus improperly encompasses more embodiments than are supported by the original disclosure."

Applicant respectfully traverses this rejection for the following reasons.

Without acquiescing to the validity of this rejection and solely in an effort to expedite prosecution and allowance of the pending claims, claim 20 has been canceled.

However, claim 15 has been amended such that the method the separating a protein A component from an immunoglobulin G component in a sample component using a selective cation-exchange adsorbent having sulphopropyl groups, comprising the steps of...". (*See Example 1, and Fig. 1*)

4. Claims 19-20 are rejected under 35 U.S.C. 112, first paragraph, as allegedly **"failing to comply with the enablement requirement.**

The Office Action maintains that:

> "...Claim 20 has not been enabled such that "only the selected ionic polymeric compound is bound to the ionic adsorbent" or "only the selected ionic biomolecule is bound to the ionic adsorbent" (e.g. the immunoglobulin that binds to the ionic adsorbent), for the case in which "only" is to be interpreted strictly."
>
> The Office Action maintains, "that the single case in which applicant exemplifies a model sample containing only previously purified IgG, protein A and buffer, the binding fraction that was subsequently eluted contained "98% IgG and 2% protein A" (Example 1). Thus the binding of "only the selected ionic polymeric compound" or "only the selected ionic biomolecule" has not been demonstrated by Applicant. The Office Action asserts that, "It is well know in the art that obtaining ion-exchange chromatographic fractions generally involve an enrichment of a "selected ionic polymeric compound" or of a "the selected ionic biomolecule", but not an exclusive purification thereof; therefore, **one would be required to conduct undue experimentation in order to separate IgG and protein A**, as in claim 20, if "only" is to be interpreted strictly. This position of the Office can be even more forcefully stated for the case in which one has a "real world" sample from a manufacturing process, rather than a model sample containing only previously purified IgG, protein A and buffer; that is, an eluate of IgG from a protein A column would be expected to contain leached protein A and trace amounts of other proteins. Also numerous protein impurities, other than the "selected' ionic biomolecule" would be present in a complex sample, such as blood, plasma/serum or culture fluid; for this reason, claim 19 is also rejected."

Applicant respectfully traverses this rejection.

Without acquiescing to the validity of this rejection and solely in an effort to expedite prosecution and allowance of the pending claims, claim 20 has been canceled.

Applicant acknowledges that protein impurities, other than the "selected' ionic biomolecule" may be present in a blood/plasma/culture sample. However, a method of separating an ionic compound of interest from a blood/plasma/culture sample having additional but different ionic compounds, occurs by using a selective cation-exchange adsorbent having a sufficiently low ionic charge density to selectively ionically bind to the ionic compound of interest. The ionic compound of interest **selectively** binds to the cation-exchange adsorbent, followed by washing the cation-exchange adsorbent with a buffered solution to remove any unbound and different ionic compounds, and followed by the application of a salt gradient of increasing conductivity applied to the cation-exchange adsorbent to ionically bind to the selected ionic compound of interest, wherein the ionically bound ionic compound of interest is eluted from the cation-exchange adsorbent.

Applicant submits that claim 19 meets the specific requirements of 35 U.S.C. §112, first paragraph, and respectfully requests reconsideration and withdrawal of each of these rejections.

E. 35 U.S.C. §102 REJECTION

1. Claims 1-2, 6 and 9-11 remain rejected under 35 U.S.C. 102(b) as allegedly being anticipated by *Wu, D. et al.*, "Effects of Stationary Phase Ligand Density On High-performance Ion-exchange Chromatography of Proteins", Journal of Chromatography 598, 7-13, 1992, (hereinafter referred to as "*Wu*"). The rejection of claims 1-2, 6 and 9 relies on the explanation in the Office Action dated May 14, 2007. The rejection of claims 10-11 relies on the explanation in the Office Action dated February 13, 2008.

The Office Action contends that the recitation of "in the absence of an additional salt that binds with the adsorbent" can be interpreted in various ways. The Office Action concurs that Fig. 2 of *Wu* was obtained under conditions in which the salt of Buffer A was present; that is, 0.01 M sodium phosphate (pH 6.0) was present (*see para. spanning pp 8-9*). However, Buffer B was absent; that is, 0.01 M sodium phos- 0.2 M sodium sulfate (pH 6.0) was not present. Thus, in the presence of only Buffer A and no Buffer B, 0.01 sodium phosphate was present, but 0.2 M sodium sulfate was absent. If one considers that the 0.2 M sodium sulfate is "an additional salt that binds with the ionic adsorbent" then this "additional salt" is absent in the binding conditions for lysozyme in Fig. 2 of *Wu* Not that the recitation in claim 1 of "in the absence of an additional salt" merely requires that a single additional salt, in this case sodium sulfate, be absent; this recitation in claim 1 does not rule out the presence of second salt, such as the 0.01 M sodium phosphate of *Wu*.

Furthermore, the Office Action considers that salt from a buffer can be present in/added to the sample since, Applicant's own teachings include the addition of a buffer to the sample in Example 1. The Office Action contends that Applicant has also urged that the examiner's arguments set forth in section 2) at page 5 of the action mailed February 13, 2008 are erroneous because the Applicant has the right to claim by way of a negative limitation. The examiner concurs that Applicant has this right; however, the negative limitation of "having a charge density that selectively binds the selected ionic component in the absence of an additional salt that binds with the adsorbent" can be interpreted in various ways. It can be interpreted as limiting the method, or it can be interpreted as limiting the nature of the adsorbent - i.e. as describing how the adsorbent would operate under the conditions in which no additional salt is present. The examiner is interpreting the negative limitation in the latter manner; thus an added salt can be present, and the negative limitation merely describes how the adsorbent would have otherwise operated (this is properly taken to be a description of the adsorbent of Wu, since their 75 umol/ml is within the range contemplated by Applicant, as being thus operative). Applicant's amendment to claim 1 does not rule out this interpretation of step a) of claim 1, because nothing in step a) says that there actually is an "absence of an additional salt" during the "contacting". Applicant may consider that the recitation of "using an adsorbent in the absence of an additional salt", as in the preamble", does rule out the actual presence of an additional salt; however, the Office need not give weight to the preamble, if there is no obligatory nexus between what is recited in the preamble and in the body of the claim. Applicant respectfully traverses this rejection for the following reasons.

THE ANTICIPATION STANDARD

The standard for anticipation is one of strict identity and "the reference must teach every aspect of the claimed invention either explicitly or inherently." (MPEP §706.02 IV, lines 6-7) Additionally, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); MPEP §2131.

Applicant's claimed invention as taught throughout the specification, see for example *paras [0008] to [0017],* is directed to a method of separating a selected ionic component from a sample by contacting the sample with an ionic adsorbent whose charge density is such that the component is bound selectively in the absence of added ionic component (salt) that competitively binds the adsorbent. Applicant has found a method of separating selected ionic components from a sample by varying the charge density of binding surfaces of an ionic adsorbent, without using an added salt in the sample as typically used in the art. The invention bypasses the need for the inclusion of competing ionic components (e.g. salts) in the sample comprising the selected ionic component while providing a highly selective method of separation. Selectivity is achieved by using an ionic adsorbent of a predetermined charge density suitable for selective binding of the ionic component of interest over a range of ionic strengths. Thus, a sample may be brought directly into contact with the adsorbent, without any costly pretreatment of the sample, since the use of large quantities of additional salts is no longer necessary.

Wu teaches cation-exchange matrices having variable ligand densities attached to a stationary phase used in high-performance ion-exchange chromatography of proteins (e.g., lysozymes and cytochrome c). High-performance ion-exchange chromatography was performed to isolate these proteins, but always in the presence of one or two additional ionic components (e.g., Na^+ salts present in either solution A or B) that also bind to the ionic adsorbent. (*see pages 8-9; and Table II).*

Applicant asserts that *Wu* fails to teach the method as claimed in **claim 1,** of separating a selected ionic protein component of interest from a sample component using a selective cation-exchange adsorbent having a sufficiently low ionic charge density to ionically bind selectively with the ionic protein component of interest which comprises the steps of (a) contacting the sample component containing the ionic protein component of interest with a selective cation-exchange adsorbent having a sufficiently low ionic charge density that binds to the ionic protein component of interest wherein the ionic charge density of the cation-exchange adsorbent is 10 to 100 μmol/ml; and (b) ionically binding the ionic protein component of interest from the sample component with the selective ionic adsorbent.

Applicant asserts that *Wu* fails to teach all of the claim elements in **claim 9,** which depends on claim 1, wherein the method according to claim 8, which further comprises step (c) washing the selective cation-exchange adsorbent with a buffered solution to remove unbound components, and step (d) applying a salt gradient of increasing conductivity to the selective

cation-exchange adsorbent and eluting the ionically bound ionic protein component of interest from the selective cation-exchange adsorbent.

Applicant asserts that *Wu* fails to teach all of the claim elements in **claims 1-2, 6 and 9-11**. As such, Applicant contends that the anticipatory rejection has been rebutted, and respectfully requests reconsideration and withdrawal of this rejection.

2. Claims 12 and 15-16 are rejected under 35 U.S.C. 102(b) as being anticipated by *Scholz, G.H. et al.,* "Salt-independent Binding of Antibodies from Human Serum to Thiophilic Heterocyclic Ligands", J. Chromatography B: Biomedical Sciences & Applications, 709:189-196, 1998 (hereinafter referred to as *"Scholz"). Scholz* was cited in the Office Action of May 14, 2007, and is being applied again "due to applicant's newly presented claims 12-20, which recite no quantitative limitation upon the ligand density, this reference is again applied."

The Office Action contends that *Scholz* teaches an immunoglobulin protein from human serum can be adsorbed to a thiophilic adsorbent, which has a binding "ligand based on mercaptonicotinic acid, containing a carboxylic group". *See last sentence of abstract, Table 3, and the para. spanning pp 195-196*, with respect to teachings of the thiophilic ligand, "Nic-S-Sulphone". This adsorption of immunoglobulin can occur in both a salt promoted and a salt-independent manner. *See sentence spanning pp 195-196.* Claims 12 and 15 are anticipated for the embodiment of *Scholz* in which the adsorption of immunoglobulin occurs in a salt independent manner. This rejection is based on the fact that claim 1 is vague and indefinite as to what is meant by the phrase "in the absence of an added salt that binds the ionic adsorbent" (112, 2nd supra), and the fact that it is not clear how this phrase relates to the teachings of the specification (112, 1st supra). In this particular rejection, the examiner interprets the phrase "*in the absence of an added salt that binds the ionic adsorbent*" as encompassing, at the least, the possible presence of an added salt that may be present in a buffering composition in added to the sample - e.g. the 25 mM sodium phosphate, pH 7.4 buffer in the case of salt free adsorption (*see p 192, col. 1).*

The Office Action contends that further noted that the "ligand based on mercaptonicotinic acid, containing a carboxylic group" has a carboxylic group that is ionized. *See para. spanning pp 195-196.* Thus adsorbent of *Scholz* is an "ionic adsorbent" as required by claims 12 and 15. The fact *Scholz* may consider that ionic binding is not the most prominent factor in the adsorption process (*para. spanning pgs 195-196*) does not detract from anticipation. That is, the adsorbent can be properly characterized as having an "ionic" group, even if the binding of immunoglobulin may be "independent of the ionic interaction of the dissociated carboxylic acid residue" (*p 196, col. 1*).

The Office Action contends that due to the fact that human serum would contain numerous proteins, other than IgG, which would not be bound/adsorbed in the method of Scholz et al, instant claims 12 and 15 are anticipated. Regarding the limitation in claims 12 and 15 concerning "charge density", this is anticipated, since there is no quantitative value recited concerning the "charge density". The Office Action contends claim 16 is anticipated since *Scholz* eluted (desorbed) IgG with NaOH. (See Table 3) Applicant respectfully traverses this rejection for the following reasons.

Applicant asserts that *Scholz* fails to teach the method as claimed in **claim 12** of separating a first ionic protein compound of interest from a sample having at least one additional different ionic protein compounds using a selective cation-exchange adsorbent having a sufficiently low ionic charge density to ionically bind to the first ionic protein compound of interest ~~a~~, comprising the steps of:

(a) contacting the sample having at least two different first and second ionic protein compounds with a selective cation-exchange adsorbent having an ionic charge density from 10 to 100 μmol/ml, wherein the ionic charge density of the cation-exchange adsorbent is selected such that the first ionic protein compound of interest binds to the cation-exchange adsorbent and the second different ionic protein compound is unbound to the cation-exchange adsorbent,

(b) washing the cation-exchange adsorbent with a buffered solution to remove the unbound second different ionic protein compound, and

(c) applying a salt gradient of increasing conductivty to the cation-exchange adsorbent and eluting the ionically bound first ionic protein compound of interest from the cation-exchange adsorbent.

Applicant further asserts that *Scholz* also fails to teach the method as claimed in **claim 15** of separating a protein A component from an immunoglobulin G component in a sample component using a selective cation-exchange adsorbent having sulphopropyl groups, comprising the steps of:(a) contacting the sample component comprising protein A and immunoglobulin G components with a selective cation-exchange adsorbent having an ionic charge density from 10 to 100 μmol/ml to ionically bind to the immunoglobulin G component, and (b) washing the selective cation-exchange adsorbent with a buffered solution to remove any unbound components.

Applicant also asserts that *Scholz* also fails to teach the method as claimed in **claim 16**, which adds step (c) to **claim 15**, of applying a salt gradient of increasing conductivty to the selective cation-exchange adsorbent, and eluting the bound immunoglobulin G from the selective cation-exchange adsorbent.

Applicant asserts that *Scholz* fails to teach all of the claim elements in **claims 1-2, 5, 7, 9-12, 14 and 19.**

As such, Applicant contends that the anticipatory rejection has been rebutted, and respectfully requests reconsideration and withdrawal of this rejection.

3. Claims 1-2, 5-7, 9-12, 14, 17 and 19 are rejected under 35 U.S.C. 102(a), (b) or (e) as allegedly being anticipated by U.S. Patent No. 6,498,236 (WO 98/08603) to *Lihme et al* (Hereinafter referred to as "*Lihme*")

The rejection is based upon 102 (a)/(e) for U.S. Patent No. 6,498,236 and under 102 (b) for the WO 98/08603. For convenience the examiner referred to the U.S. Patent No. 6,498,236 by col. and line number. The Office Action contends that *Lihme* teaches chromatographic

adsorbents/matrices which **have a negative charge on their surface** due to the presence of a COOH group attached to an aromatic ring. This group would be ionized at the taught pK range values for the COOH group and the taught pH ranges values for adsorption (*e.g. see col. 8, lines 46-65 and col. 15, lines 25-41).* For the exemplified 2-mercaptobenzoic acid (2-MBA), the pH values at which binding of immunoglobulins are in the acid range, where the COOH group would be ionized *(e.g. col. 31, lines 27-59).* For the exemplified 2-amino-benzoic acid (4-ABA), the pH values at which binding of immunoglobulins are in the acid range, where the COOH group would be ionized (*e.g. col. 35, lines 1-52*). For the exemplified 2 mercapto-nicotinic acid, the pH values at which binding of immunoglobulins are in the acid range, where the COOH group would be ionized (e.g. *col. 36, lines 1-50*). The operative ligand densities are taught at *col. 18, lines 17-32; col. 30, lines 29-34; col. 34, lines 62-67; col. 35, lines 62-6.*

The Office Action contends the exemplified separations of IgG from an "Artificial Culture Supernatant" *(col. 30, lines 30+)* and from sera (*col. 38, lines 9+)* most certainly show the separation of a "selected" IgG from "additional ionic components", other "ionic polymeric compounds" (e.g. in the fetal calf serum of the "Artificial Culture Supernatant"), or a second "ionic biomolecule", thereby anticipating the instant claims 1-2, 5-7, 10-12, 14-15 and 17. As to claims 9 and 16, the Office Action notes that *Lihme* elutes the adsorbed IgG (*e.g. col. 4,*

lines 30-33; col. 7, lines 19-47; col. 30, lines 56-61; col. 32, lines 19-61; col. 35, lines 31-53).

Regarding claim 19, the Office Action contends it is taken that the exemplification of purification of IgG from an Artificial Culture Supernatant" would permit one of skill to immediately envision "cell culture broth" sample, also citing *Lihme at col. 9, lines 18-26.* The Office Action contends that *Lihme* adds a buffer to the "Artificial Culture Supernatant" samples, prior to contacting these samples with the adsorbent/matrix (*e.g. col. 29, lines 34-38*). Such addition of buffer would add salt to the sample; however, the Office considers that such addition is permitted, since applicant's own teachings in Example 1 include the addition of a buffer to the sample. Applicant respectfully traverses this rejection for the following reasons.

Applicant asserts that *Lihme* fails to teach the method as claimed in **claim 1,** of separating a selected ionic protein component of interest from a sample component using a selective cation-exchange adsorbent having a sufficiently low ionic charge density to ionically bind selectively with the ionic protein component of interest which comprises the steps of (a) contacting the sample component containing the ionic protein component of interest with a selective cation-exchange adsorbent having a sufficiently low ionic charge density that binds to the ionic protein component of interest wherein the ionic charge density of the cation-exchange adsorbent is 10 to 100 µmol/ml; and (b) ionically binding the ionic protein component of interest from the sample component with the selective ionic adsorbent.

Applicant asserts that *Lihme* fails to teach the method as claimed in **claim 2,** which depends on **claim 1,** wherein the selective ionic adsorbent is a cation-exchange adsorbent.

Applicant asserts that *Lihme* fails to teach the method as claimed in **claim 14,** which depends on **claim 12,** wherein the cation-exchange adsorbent has an ionic charge density from 30 to 80 µmol/ml and comprises agarose beads having sulphopropyl groups.

Applicant also asserts that *Lihme* fails to teach the method as claimed in **claim 19**, which depends on **claim 15**, wherein the sample component is selected from the group consisting of blood and cell culture broths.

Applicant asserts that *Lihme* fails to teach all of the claim elements in **claims 1-2, 5, 7, 9-12, 14 and 19.**

As such, Applicant contends that the anticipatory rejection has been rebutted, and respectfully requests reconsideration and withdrawal of this rejection.

4. Claims 12 and 14-16 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by *Hahn et al.* (Jour. Chromat. A., 795, 277-287, 1998), (hereinafter referred to as "*Hahn*").

The Office Action contends that *Hahn* teaches a sample of bovine whey prepared by addition of HCL to milk, in order to precipitate casein, which is then removed by centrifugation. The thus obtained whey was diluted with water to a conductivity of 2.7 mS/cm. The Office Action contends that the preparation of whey as indistinguishable from that exemplified by applicant (example 2). See *Hahn* at *para. spanning pp 278-279*. Thus it is properly considered that no salt was added that would bind to the ionic adsorbent. The thus prepared whey is then contacted with one of various cation-exchange resins, including S-Sepharose FF (*p 278, col.* 2) under conditions such that IgG bound to the adsorbent and alpha-lactalbumin passes through the column (para. spanning pp 280-281). Thus there is a separation "of a selected ionic polymeric compound from a sample having at least two ionic polymeric compounds" or of "of a selected ionic biomolecule from a sample having at least two ionic biomolecules". The Office Action contends that claims 12, 14-15 and 17 are anticipated. Regarding claim 16, *Hahn* then elutes the bound IgG (*see pp 281-282*).

Applicant asserts that *Hahn* fails to teach all of the claim elements in **claims 12 and 14-16.**

Applicant asserts that *Hahn* fails to teach the method as claimed in **claim 12** of separating a first ionic protein compound of interest from a sample having at least one additional different ionic protein compounds using a selective cation-exchange adsorbent having a sufficiently low ionic charge density to ionically bind to the first ionic protein compound of interest ~~a~~, comprising the steps of:**(a)** contacting the sample having at least two different first and second ionic protein compounds with a selective cation-exchange adsorbent having an ionic charge density from 10 to 100 µmol/ml, wherein the ionic charge density of the cation-exchange adsorbent is selected such that the first ionic protein compound of interest binds to the cation-exchange adsorbent and the second different ionic protein compound is unbound to the cation-exchange adsorbent,**(b)** washing the cation-exchange adsorbent with a buffered solution to remove the unbound second different ionic protein compound, and **(c)** applying a salt gradient of increasing conductivty to the cation-exchange adsorbent and eluting the ionically bound first ionic protein compound of interest from the cation-exchange adsorbent.

Applicant further asserts that *Hahn* fails to teach the method as claimed in **claim 15** of separating a protein A component from an immunoglobulin G component in a sample

component using a selective cation-exchange adsorbent having sulphopropyl groups, comprising the steps of:(a) contacting the sample component comprising protein A and immunoglobulin G components with a selective cation-exchange adsorbent having an ionic charge density from 10 to 100 μmol/ml to ionically bind to the immunoglobulin G component, and (b) washing the selective cation-exchange adsorbent with a buffered solution to remove any unbound components.

Applicant also asserts that *Hahn* also fails to teach the method as claimed in **claim 16**, which adds step (c) to **claim 15**, of applying a salt gradient of increasing conductivty to the selective cation-exchange adsorbent, and eluting the bound immunoglobulin G from the selective cation-exchange adsorbent.

As such, Applicant contends that the anticipatory rejection has been rebutted, and respectfully requests reconsideration and withdrawal of this rejection.

F. 35 U.S.C. §102/103 REJECTION

5. Claims 1, 5-6, 9-12 and 15-16 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over U.S. Patent No. 4,883,598 to *Reithorst et al.* (hereinafter referred to as "*Reithorst*")

The Office Action contends that *Reithorst* teaches anion exchange matrices/adsorbents that have a ligand density that is "preferably higher than 30 umoles/ml, more preferably higher than 50 umoles/ml and most preferably 60-100 umoles/ml of swollen gel" *(col. 8, lines 24-28)*. They disclose numerous matrices/adsorbents that have a ligand density in the range from 40-80 umoles/ml (*Tables 1-9*), which are within applicant's recited ranges of "10 to 100", "20 to 90" and "30 to 80 umol/ml". These matrices are used for the selective adsorption and elution of various blood coagulation factors, such as Factor VIII and vVF (*col. 6, lines 26-34; col. 9, lines 27-45)*. These are isolated from plasma samples, which would contain some low concentration of a salt, due to the addition of an anti-coagulant (e.g. sodium citrate). These samples also contain salt due to the presence of an acetate/lysine buffer. *See col. 15, line 40-col. 16, line 15.* The Office considers that such addition of anticoagulant/buffer salt is permitted, since applicant's own teachings in Example 1 include the addition of buffer salt to the sample. From the above, instant claims 1, 5-6, 9-12 and 15-16 are anticipated or obvious. The examiner considers that the claims are anticipated; however, an obviousness rejection is made in the alternative (e.g. in the event that applicant should argue the limits of the preferred ranges taught by *Reithorst.* Applicant respectfully traverses these rejections for the following reasons.

Applicant asserts that *Reithorst* fails to teach the method as claimed in **claim 1,** of separating a selected ionic protein component of interest from a sample component using a selective cation-exchange adsorbent having a sufficiently low ionic charge density to ionically bind selectively with the ionic protein component of interest which comprises the steps of (a) contacting the sample component containing the ionic protein component of interest with a selective cation-exchange adsorbent having a sufficiently low ionic charge density that binds to the ionic protein component of interest wherein the ionic charge density of the cation-exchange

adsorbent is 10 to 100 μmol/ml; and (b) ionically binding the ionic protein component of interest from the sample component with the selective ionic adsorbent.

Applicant asserts that *Reithorst* fails to teach all of the claim elements in **claim 5**, which depends on claim 2 [wherein the selective ionic adsorbent is a cation-exchange adsorbent], wherein the sample component comprises an additional ionic protein component, and the ionic charge density of the selective cation-exchange ionic adsorbent is selected such that the additional ionic protein component is not ionically bound to the selective cation-exchange ionic adsorbent.

Applicant asserts that *Reithorst* fails to teach all of the claim elements in **claim 9**, which depends on claim 1, wherein the method according to claim 8, which further comprises step (c) washing the selective cation-exchange adsorbent with a buffered solution to remove unbound components, and step (d) applying a salt gradient of increasing conductivity to the selective cation-exchange adsorbent and eluting the ionically bound ionic protein component of interest from the selective cation-exchange adsorbent.

Applicant asserts that *Reithorst* fails to teach all of the claim elements in **claim 10**, which depends on claim 2, wherein the ionic charge density of the selective cation-exchange ionic adsorbent is from 20 to 90 μmol/ml.

Applicant asserts that *Reithorst* fails to teach all of the claim elements in **claim 11**, which depends on claim 1, wherein the ionic charge density of the selective cation-exchange ionic adsorbent is from 30 to 80 μmol/ml.

Applicant further asserts that *Reithorst* also fails to teach the method as claimed in **claim 15** of separating a protein A component from an immunoglobulin G component in a sample component using a selective cation-exchange adsorbent having sulphopropyl groups, comprising the steps of:(a) contacting the sample component comprising protein A and immunoglobulin G components with a selective cation-exchange adsorbent having an ionic charge density from 10 to 100 μmol/ml to ionically bind to the immunoglobulin G component, and (b) washing the selective cation-exchange adsorbent with a buffered solution to remove any unbound components.

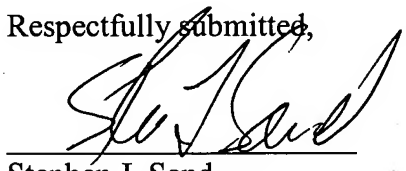
Applicant asserts that *Reithorst* fails to teach all of the claim elements in **claims 1, 5, 9-12 and 15-16**, and respectfully contends that the anticipatory rejection has been rebutted, and requests reconsideration and withdrawal of this rejection.

Applicant respectfully asserts that the Office Action has failed to establish a *prima facie* case of obviousness. *Reithorst* does not teach or suggest all of the claim elements, therefore, do not establish a *prima facie* case of obviousness.

IV. CONCLUSION

In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejections, and the timely allowance of the pending claims. Applicant believes that the above response is a complete response to the present office action. If however the Examiner believes that some requirement has been missed or not completely answered, the Examiner is invited to contact Applicant's attorney at the number below. Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account.

Respectfully submitted,



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